Leading the Attack on Cancer

LAST October, Lawrence Livermore joined forces with the University of California at Davis Cancer Center to fight cancer, the nation's second leading killer. Together, they are researching cancer biology, prevention, and control as well as new cancer detection and treatment techniques.

During a ceremony to announce the collaboration, Livermore Deputy Director for Science and Technology Jeff Wadsworth noted that the collaboration reflects the principles on which Ernest Lawrence founded the Laboratory. "One of those principles was that the Laboratory should work on problems of national importance using multidisciplinary teams on projects of scale," he said. "I think this collaboration exemplifies those principles. Solutions to cancer are of great national importance, and we're using multidisciplinary teams from this Laboratory and UC Davis in this effort."

Livermore brings to the venture its multidisciplinary staff of scientists and engineers, supercomputing expertise, and a biomedical research program that dates back to the early 1960s. The UC Davis Cancer Center contributes its patient-centered research and clinical experience. The collaboration offers a clinical testing ground for medical technologies that Livermore develops.

Over the years, Livermore has developed expertise in DNA repair, cancer susceptibility, dietetic carcinogenesis, genetic toxicology, structural biology, genomics, and biotechnology. Livermore in collaboration with Lawrence Berkeley and Los Alamos national laboratories formed the Joint Genome Institute to decode three chromosomes for the Human Genome Project. Livermore is also one of the few research institutions in the world that is applying accelerator mass spectrometry to biological research (see *S&TR*, November 1997, pp. 4–11, and July/August 2000, pp. 12–19). With this ultrasensitive measuring technique, most commonly used to trace carbon-14 in samples for carbon dating, scientists can for the first time measure how typical doses of a suspected carcinogen affect DNA. Scientists from Livermore and UC Davis are already using it to learn more about how we metabolize vitamins and other nutrients.

Scientists from UC Davis and Livermore have been performing research together for several years. A few Livermore scientists are already adjunct professors at UC Davis. This collaboration brings the two organizations together on a more formal basis, making it easier for these two parts of the University of California to work together in the future. Under the terms of the agreement, molecular biologist Jim Felton, a Livermore specialist in cancer causation and prevention, and physicist Dennis Matthews, leader of Livermore's Medical Technology Program, have been named associate directors of the UC Davis Cancer Center. Felton is also the Livermore liaison to UC Davis for all work associated with the collaboration.

Much Work in Progress

Together, Lawrence Livermore and the UC Davis Cancer Center have about 200 scientists and physicians working on cancer research projects. Their work falls into six areas: molecular oncology; cancer biology in animals; cancer therapeutics; cancer etiology (causation), prevention, and control; prostate cancer; and biomedical technologies. Each research area has 25 or more researchers involved, with participants from both Livermore and UC Davis.

Livermore researchers are participating in all six research areas and are taking a leadership role in three of them. Felton

Lawrence Livermore National Laboratory

is co-leader of research on cancer causation, prevention, and control. Matthews is co-leading the work on biomedical technology. Toxicologist Ken Turtletaub is co-leader of molecular oncology research.

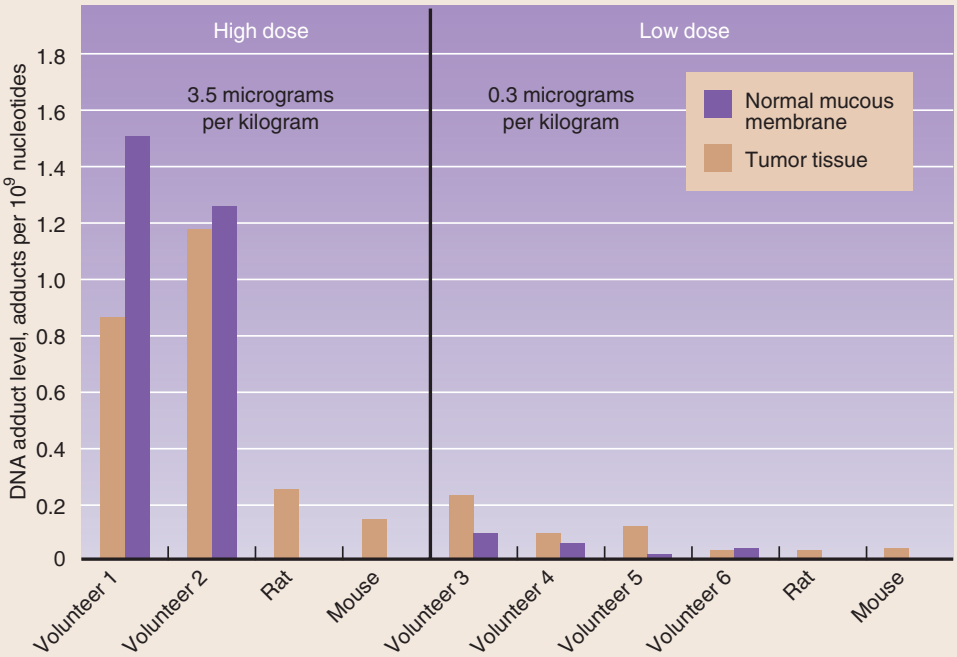
The team headed by Felton and Marc Schenker, M.D., of UC Davis seeks to better understand the causes of cancer and then to develop and implement strategies to reduce cancer incidence and morbidity. Their work focuses on three causes of cancer—tobacco, nutrition, and environmental exposures. For many years, Felton has been studying the effects of diet on carcinogenesis, in particular, how heterocyclic amines produced during the cooking of meats may damage DNA and ultimately cause cancer. Other joint dietary studies are examining the role of selenium and folate in preventing cancer. Says Felton, "We are also tackling the effects of tobacco smoke constituents on rodent and human lung cells and tissue. Working with the California State Department of Public Health, we are studying methods to convince people to stop smoking."

Under Matthews and UC Davis Professor of Radiology John Boone, the biomedical technology program combines expertise in physical and life sciences and engineering to create new devices and technologies. The emphasis is on imaging and diagnostics research and the development of therapeutic devices. About 20 projects are under way in these areas. For example, using ultrashort-pulse technology developed at Livermore, a joint team is developing a diagnostic tool that creates images showing melanomas and other cancers on the surface of the skin. One therapeutic device is PEREGRINE, a new approach developed at Livermore to planning radiation therapy for treating cancer (*S&TR*, May 1997, pp. 4–11, and October 1999, pp.14–15). PEREGRINE was recently cleared by the U.S. Food and Drug Administration for use in clinics and hospitals. The project team has turned its attention to developing imaging simulation codes as well as the means to plan radiation therapy using internal radiation sources.

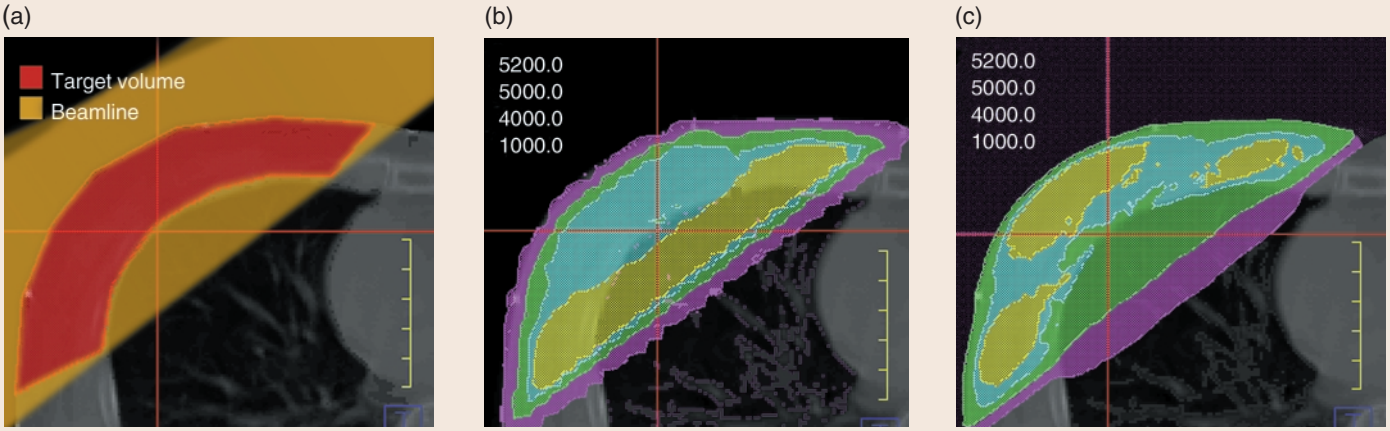
Turtletaub and molecular biologist Hsing-Jien Kung of UC Davis are managing research on molecular oncology. They are examining the fundamental processes of cancer biology from the initial "insult" to the cell through the intermediate and later responses of the cell, be they negative effects of the carcinogen or the healing effects of therapy. Turtletaub is overseeing the work related to DNA damage and cycle checkpoints, continuing a long-term study of DNA damage and repair. The team hopes to quickly translate its discoveries about cancer mechanisms into the development of prognostic markers and curative therapies.

A New Approach to Commercialization

Livermore is taking a new approach to getting its technologies commercialized and available for use by physicians and patients. Along the lines of the joint cancer center, Livermore and UC Davis have initiated a joint Bio



In earlier work, Livermore researchers found that rodents and humans exhibit significantly different responses to high and low doses of MelQx, a chemical that appears in meat after it is cooked. MelQx causes damage to DNA. Scientists from Livermore and the University of California at Davis will continue this work and perform similar experiments to determine the effects of tobacco on humans and rodents.



This breast cancer case highlights the importance of accurate dose calculations for correct dose coverage of a tumor and sensitive surrounding lung tissue. (a) The radiation applied to the target is shown in general. (b) While conventional dose calculations show that the prescribed dose level covers the entire tumor, (c) PEREGRINE calculations suggest that for this treatment, the prescribed dose shows a higher skin dose, deeper penetration of dose into the lung, and a different dose distribution within the chest wall.

and Medical Technology Development Industrial Partners Consortium. By working together, Livermore, the UC Davis Health System, and industrial partners form a complete "laboratory bench-to-bedside" cycle for innovative medical technologies. Livermore's Medical Technology Program and Biology and Biotechnology Research Program and the UC Davis Health System are experienced in identifying critical medical needs, researching new concepts, and developing prototype devices. The industrial partners will develop these devices into commercial products, shepherd them through the approval process, and distribute them to the medical profession.

Formed at about the same time as the joint cancer center, the Industrial Partners Consortium is not limited to technologies related to cancer. More than 50 participants from 30 companies attended the first presentation by the consortium in November 2000. Since then, numerous companies have expressed interest in working with Livermore and UC Davis, and one partnership has officially been formed.

Toward Becoming an NIH Cancer Center

Another major goal for the Livermore and UC Davis collaboration is to become a designated cancer center by the National Cancer Institute (NCI). One of the National Institutes of Health, NCI funds 60 cancer centers throughout the U.S. These centers emphasize multidisciplinary cancer research as well as public information, education, and outreach. NCI's decision on the collaboration's application to become a designated cancer center is expected in the fall of 2001.

NIH funding would not be for specific projects but for overhead support and would thus free many scientist–administrators to perform more actual research. The funding would also help initiate collaborations between institutions and provide seed money for new areas of research that support the six themes of the cancer center.

Cancer has or will touch the lives of almost everyone in the country at some time. Yet only about half of all newly diagnosed cancer patients can be treated effectively with available therapies. Increasing that percentage—and finding better ways to prevent, detect, and diagnose the disease—will benefit us all.

—Katie Walter

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